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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/955,383 | 09/18/2001 | Neng-Yang Shih | AL01019 | 8337 |

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PATENT DEPARTMENT (K-6-1, 1990)
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| EXAMINER | |
|---|---|
| LIU, HONG | |
| **ART UNIT** | **PAPER NUMBER** |
| 1624 | |

DATE MAILED: 03/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application N . | Applicant(s) | |
|---|---|---|---|
| | 09/955,383 | SHIH ET AL. | |
| | Examiner | Art Unit | |
| | Hong Liu | 1624 | |

*-- The MAILING DATE of this communicati n app ars on the cover sheet with the c rresp ndence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *5,8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4,6,7 and 10-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Claims 1-18 are pending in this application.

### *Election/Restrictions*

1: Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-18, drawn to the compounds of formula I wherein one of X and Y is N, the other is CH, M is a moiety having the structure shown in formula II, the compositions and methods of use, classified in class 544, subclass 194.

II. Claims 1-18, drawn to the compounds of formula I wherein one of X and Y is N, the other is CH, M is a moiety having the structure shown in formula III, the compositions and methods of use, classified in classes 546 or 548, subclasses depending on the variables of M, X, or Y.

III. Claims 1-18, drawn to the compounds, composition, and methods of use not included in Groups I and II, classified in classes and subclasses depending on the nature of the substituents.

The inventions are distinct, each from the other because of the following reasons:

Groups I, II, and III are directed to structurally dissimilar compounds such that the variable core created by varying the definitions of the formula do not belong to a recognized class of chemical compounds in the art, and references anticipating one invention would not render obvious the others, for example, piperidine or piperazine, etc. are different from phenyl. Thus, separate searches in the literature as well as in the U.S. Patent Clarification System would be required. Each group's compounds are made and used independently of each other and could support separate patents. The compounds differ significantly in chemical structures. One skilled

in the art would not consider such diverse structures as functional equivalents of each other. The mere fact that there is a single similarity is not in itself a significant reason to render the whole embodiment obvious.

2. During a telephone conversation with Dr. Palaiyur Kalyanaraman on 02/14/03 a provisional election was made with traverse to prosecute the invention of group I, claims 1-18. Affirmation of this election must be made by applicant in replying to this Office action. Claims 5, 8, and 9 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 1-4, 6, 7, 10-18 are objected to as being an improper Markush grouping. The recited compounds, while possessing a common utility, present a variable core and, thus, the Markush groups represented by the term where X and Y are both carbon or nitrogen, M is of formula III have variably different definitions, render the claims clearly improper.

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-4, 6, 7, 10-15, and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preparation of compounds wherein M is piperidine or piperazine, does not reasonably provide enablement for preparation and use of compounds wherein M is other than the above specified functional groups. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The nature of the invention in the instant application has claims which embrace a diversity of chemically and physically distinct compounds, wherein p and q is 0, 1, or 2, Z is CH or N, etc. While many compounds are disclosed, there is insufficient guidance for preparing additional "H3 receptor antagonists" which would be effective since the cited examples are drawn to a homogenous group of compounds not remotely commensurate in scope to applicants' claims. Only compounds wherein M is piperidine or piperazine have been made. There is no teaching in the specification how to make the compounds using starting materials not containing piperidine or pierazine.

Furthermore, testing data is limited to a number of compounds not considered to be representative of all the possible compounds encompassed by the claims. Examples should be of sufficient scope as to justify the scope of the claim. However, the generic claims are much broader in scope than is represented by the testing. The definitions of the various p, q and Z variables embrace many structurally divergent groups not represented at all in testing, since testing for the instant compounds is not seen in the specification. Markush claims must be provided with support in the disclosure when the "working examples' fail to include written

description(s) which teach how to make and use Markush members embraced thereby in full, clear and exact terms. See In re Fouch, 169 USPQ 429.

This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically-based pharmacological activity. In view of the structural divergence in the claims, one skilled in the art could not reasonably extrapolate the activities of some of the claimed compounds to the other structurally divergent compounds embraced by the claims which have not been tested. In cases directed to chemical compounds which are being used for their physiological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. No reasonable assurance has been made that the instant compounds as an entire class have the required activities needed to practice the invention. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability" have been demonstrated to be sufficiently lacking in the instant case.

Claims 13-15 and 18 are drawn to a method of treating various diseases associated with H3 receptor. The treatment includes inflammation, allergy, nasal congestion, diseases of the GI-tract, cardiovascular disease, or disturbances of the central nervous system, obesity, etc. However, in a review article about histamineH3- receptor, provided by applicants, Leurs and Timmerman stated the H3-receptor agents might be useful for only airway and gastrointestinal disorders (p162, Drug Res. 1992), Additionally, no evidence of in vitro/in vivo effectiveness is seen in the specification for one of the (let alone all) of the instant compounds for the uses claimed herein. See In re Surrey, 252 USPQ 724, regarding sufficiency of disclosure. Competent evidence of art-recognized efficacy for intended uses needs to be provided. Any evidence

presented must be commensurate in scope with the claims and must clearly demonstrate the likelihood of in vivo use for all uses being claimed. See Ex parte Powers, 220 USPQ 925. scope being claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 11, 12, 14, 16, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1). In claims 1, 16, 17, the word "including" is open-ended. The claims are vague and indefinite in that the metes and bounds of the word is unknown.

2).The phrase "substituted or unsubstituted" for R7 and R8 in claim 1 is unclear as to the nature and number of substituent(s) intended.

3). Claims 11 is a substantial duplicate of Claim 12, as the only difference is intended use which is not given material weight. Note In re Tuominen 213 USPQ 89. Claim 10 is a substantial duplicate of claim 12 as the scope of these claims are the same.

4). Claim 14 provides for the use of the compounds, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 14 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e.,

results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Liu whose telephone number is 703 3065814. The examiner can normally be reached on 8:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703 308 4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703 308-4556 for regular communications and 703 3084734 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 358-1235.

RICHARD L. RAYMOND
PRIMARY EXAMINER
ART UNIT 1624

**Mukund Shah**
**Supervisory Patent Examiner**
**Art Unit 1624**

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March 10, 2003